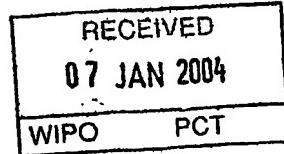


10/533,346



P1 1108422

THE UNITED STATES OF AMERICA

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December 31, 2003

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APPLICATION THAT MET THE REQUIREMENTS TO BE GRANTED A  
FILING DATE.

APPLICATION NUMBER: 60/422,465

FILING DATE: *October 30, 2002*

RELATED PCT APPLICATION NUMBER: PCT/US03/34442

By Authority of the  
COMMISSIONER OF PATENTS AND TRADEMARKS

  
*H. L. Jackson*  
H. L. JACKSON  
Certifying Officer

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**PROVISIONAL APPLICATION FOR PATENT COVER SHEET**

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53(c).

Express Mail Label No.

EV 094 353 450 US

**INVENTOR(S)**

Given Name (first and middle [if any])	Family Name or Surname	Residence (City and either State or Foreign Country)
Terry L.	Sheehan	Walnut Creek, California

 Additional Inventors are being named on the \_\_\_\_\_ separately numbered sheets attached hereto**TITLE OF THE INVENTION (500 characters max)**

PROGRAMMABLE TEMPERATURE AND FLOW OF NEBULIZATION AND DRYING GASES UTILIZED IN ATMOSPHERIC PRESSURE IONIZATION (API) INTERFACES FOR MASS SPECTROMETRY

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PATENT TRADEMARK OFFICE

**ENCLOSED APPLICATION PARTS (check all that apply)**

<input checked="" type="checkbox"/> Specification Number of Pages	2	<input type="checkbox"/> CD(s), Number	
<input type="checkbox"/> Drawing(s) Number of Sheets		<input type="checkbox"/> Other (specify)	
<input type="checkbox"/> Application Data Sheet. See 37 CFR 1.76			

**METHOD OF PAYMENT OF FILING FEES FOR THIS PROVISIONAL APPLICATION FOR PATENT**

<input type="checkbox"/> Applicant claims small entity status. See 37 CFR 1.27.	FILING FEE AMOUNT (\$)
<input type="checkbox"/> A check or money order is enclosed to cover the filing fees	
<input checked="" type="checkbox"/> The Commissioner is hereby authorized to charge filing fees or credit any overpayment to Deposit Account Number: 50-0895	\$160.00
<input type="checkbox"/> Payment by credit card. Form PTO-2038 is attached.	

The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.

 No. Yes, the name of the U.S. Government agency and the Government contract number are: \_\_\_\_\_Respectfully submitted,  
*Bella Fishman*

Date 10/30/2002

SIGNATURE

TYPED or PRINTED NAME Bella Fishman

TELEPHONE 650.424.5086

REGISTRATION NO.  
(If appropriate)  
Docket Number:

37,485

02-40 PRO

**USE ONLY FOR FILING A PROVISIONAL APPLICATION FOR PATENT**

This collection of information is required by 37 CFR 1.51. The information is used by the public to file (and by the PTO to process) a provisional application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 8 hours to complete, including gathering, preparing, and submitting the complete provisional application to the PTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Box Provisional Application, Assistant Commissioner for Patents, Washington, D.C. 20231.

Title of Invention: Programmable temperature and flow of nebulization and drying gases utilized in atmospheric pressure ionization (API) interfaces for mass spectrometry

Inventor: Terry L. Sheehan

A. *Brief statement of the invention:* Programmable temperature and flow of the nebulization and drying gases to maximize the droplet formation and evaporation (desolvation) as mobile phase composition changes across the gradient applied to the liquid chromatographic column.

B. *the features of the invention*

Existing API interfaces use constant conditions for flow and temperature of the gases which creates performance compromises at the extremes of the LC gradient composition.

C. *Brief description of the preferred and alternative embodiments,*

Assuming electronic flow of gases, the software would have to be modified to drive the appropriate increase/decrease in temperature and flow during the course of the compositional gradient from the liquid chromatograph.

D. *the advantages of the invention or problems solved by the invention:*

With fixed temperature and flow of API gases, optimal efficiency of droplet evaporation is only achieved for a single composition of liquid chromatographic solvents. For isocratic (constant LC mobile phase conditions) separations, these fixed conditions for the gases are acceptable. There has, however, been a steadily shift in all LC/MS market segments toward gradient separations. Fixed conditions for the gases results in less than optimal efficiency in the API interface as mobile phase conditions deviate from the single composition that was used to setup the analysis.

Programmable control of the gases (flow and temperature) will compensate for changes in droplet surface tension, mobile phase viscosity, and mobile volatility. Two net benefits exist: (1) better signal for all analytes across the gradient separation through optimal evaporation of droplets and (2) less

opportunity for thermal degradation of analytes under gas conditions that are too aggressive for a mobile phase composition associated with that analyte. These benefits should be realized for any API Interface that follows the basic design of electrospray or chemical ionization.

- E. *List of prior art (previous) methods, materials, or devices relating to the invention:* API interfaces current employ both nebulization and drying gases under fixed conditions for flow and temperature.

## PATENT COOPERATION TREATY

**PCT**

REC'D	21 FEB 2005
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## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference <b>02-40 PCT</b>	<b>FOR FURTHER ACTION</b>	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. <b>PCT/US03/34442</b>	International filing date (day/month/year) <b>29 October 2003 (29.10.2003)</b>	Priority date (day/month/year) <b>30 October 2002 (30.10.2002)</b>
International Patent Classification (IPC) or national classification and IPC <b>IPC(7): G01N 30/72; B01D 15/08 and US Cl.: 436/161; 422/70; 210/656, 198.2</b>		
Applicant <b>VARIAN, INC.</b>		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 3 sheets, including this cover sheet.

This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of \_\_\_ sheets.

3. This report contains indications relating to the following items:

- I  Basis of the report
- II  Priority
- III  Non-establishment of report with regard to novelty, inventive step and industrial applicability
- IV  Lack of unity of invention
- V  Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI  Certain documents cited
- VII  Certain defects in the international application
- VIII  Certain observations on the international application

Date of submission of the demand <b>14 May 2004 (14.05.2004)</b>	Date of completion of this report <b>07 February 2005 (07.02.2005)</b>
Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPBA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Jan M. Ludlow DEBORAH A. THOMAS PARALEGAL SPECIALIST Telephone No. (703) 308-0661 <i>GROUP 1900 Pct</i>

Form PCT/IPEA/409 (cover sheet)(July 1998)

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US03/34442

**I. Basis of the report**

## 1. With regard to the elements of the international application:\*

 the international application as originally filed. the description:pages 1-17 as originally filedpages NONE, filed with the demandpages NONE, filed with the letter of \_\_\_\_\_. the claims:pages 18-21, as originally filedpages NONE, as amended (together with any statement) under Article 19pages NONE, filed with the demandpages NONE, filed with the letter of \_\_\_\_\_. the drawings:pages 1-2, as originally filedpages NONE, filed with the demandpages NONE, filed with the letter of \_\_\_\_\_. the sequence listing part of the description:pages NONE, as originally filedpages NONE, filed with the demandpages NONE, filed with the letter of \_\_\_\_\_.

## 2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

 the language of a translation furnished for the purposes of international search (under Rule 23.1(b)). the language of publication of the international application (under Rule 48.3(b)). the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

## 3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

 contained in the international application in printed form. filed together with the international application in computer readable form. furnished subsequently to this Authority in written form. furnished subsequently to this Authority in computer readable form. The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished. The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.4.  The amendments have resulted in the cancellation of: the description, pages NONE the claims, Nos. NONE the drawings, sheets/fig NONE5.  This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\* Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.  
PCT/US03/34442

## V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

## 1. STATEMENT

Novelty (N)

Claims 1-22 YES  
Claims NONE NO

Inventive Step (IS)

Claims 1-22 YES  
Claims NONE NO

Industrial Applicability (IA)

Claims 1-22 YES  
Claims NONE NO

## 2. CITATIONS AND EXPLANATIONS

Claims 1-22 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest a method or apparatus for LC/MS with API in which the chromatography is conducted with gradient elution, and the temperature or flow rate of vaporizing gas is varied in accordance with the gradient.

Note that VESTAL (4,958,529) does not teach or suggest gradient elution.

Claims 1-22 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

— NEW CITATIONS —

## INTERNATIONAL SEARCH REPORT

PCT/US 03/34442

**A. CLASSIFICATION OF SUBJECT MATTER**  
 IPC 7 G01N30/72 B01D15/08

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
 IPC 7 B01D G01N H01J

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 958 529 A (VESTAL MARVIN L) 25 September 1990 (1990-09-25) column 14, line 28 -column 15, line 16; claims 17-19; figures 3,5 ---	1-22
A	US 4 814 612 A (VESTAL MARVIN L ET AL) 21 March 1989 (1989-03-21) claims; figures 1-3 ---	1-22
A	US 5 412 208 A (ANACLETO JOSEPH F ET AL) 2 May 1995 (1995-05-02) column 4, line 33 -column 5, line 25; claims; figure 2 ---	1-22
A	US 6 339 218 B1 (KATO YOSHIAKI ET AL) 15 January 2002 (2002-01-15) column 11, line 3 - line 17; claims ---	1-22 -/-



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

## \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the International filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the International filing date but later than the priority date claimed

- \*T\* later document published after the International filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed Invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed Invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the International search

18 February 2004

Date of mailing of the International search report

25/02/2004

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
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Fax (+31-70) 340-3016

Authorized officer

Fourgeaud, D

## INTERNATIONAL SEARCH REPORT

PCT/US 03/34442

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,A	US 6 484 560 B1 (PREST HARRY F) 26 November 2002 (2002-11-26) column 7, line 32 - line 47; figures 2A-2C -----	1-22

## INTERNATIONAL SEARCH REPORT

PCT/US 03/34442

Patent document cited in search report		Publication date		Patent family member(s)		Publication date
US 4958529	A	25-09-1990	NONE			
US 4814612	A	21-03-1989	US CA US US	4960992 A 1227950 A1 4861989 A 4730111 A		02-10-1990 13-10-1987 29-08-1989 08-03-1988
US 5412208	A	02-05-1995	AU CA WO DE DE EP	1410295 A 2181040 A1 9519638 A2 69509359 D1 69509359 T2 0739533 A1		01-08-1995 20-07-1995 20-07-1995 02-06-1999 14-10-1999 30-10-1996
US 6339218	B1	15-01-2002	JP JP US JP JP US US	3087548 B2 7159377 A 5859432 A 3379510 B2 2000314726 A 5581081 A 6236042 B1		11-09-2000 23-06-1995 12-01-1999 24-02-2003 14-11-2000 03-12-1996 22-05-2001
US 6484560	B1	26-11-2002	NONE			

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